Disease Name — 3-methylcrotonyl-CoA carboxylase deficiency

Alternate name(s)	3-methylcrotonylglycinuria
Acronym	3-MCC
Disease Classification	Organic Acid Disorder
Variants	Late-onset form
Variant name	Late-onset 3-methylcrotonyl-CoA carboxylase deficiency
Symptom onset	Many individuals remain asymptomatic into adulthood. Others present in late infancy (generally after 3 months).
Symptoms	Infants can present with a Reye-like syndrome of ketoacidosis, hypoglycemia, hyperammonemia which can lead to seizures, coma and possibly death. Others present with failure to thrive, hypotonia or spasticity. Late-onset 3-MCC may present as developmental delay without Reye-like syndrome. Symptomatic adults often report general weakness and fatigue. Many individuals are asymptomatic.
Natural history without treatment	Primary manifestations appear to be muscular hypotonia and atrophy. Individuals with Reye-like illnesses may die or suffer neurologic insult during these episodes.
Natural history with treatment	Once over the initial crisis, most individuals have been intellectually normal. It is uncertain whether treatment modifies disease course.
Treatment	Protein restricted diet. Leucine-free medical foods. Possible carnitine supplementation. Giving treatment to asymptomatic individuals is of questionable value.
Other	Newborn screening has led to the diagnosis of asymptomatic women whose infants have transiently elevated isovalerylcarnitine.
Physical phenotype	None
Inheritance	Autosomal recessive
General population incidence	1:50,000
Ethnic differences	No known population at increase risk
Population	N/A
Ethnic incidence	N/A
Enzyme location	Inner membrane of the mitochondria, liver and kidney.
Enzyme Function	Breakdown of leucine
Missing Enzyme	3-methylcrotonyl-CoA carboxylase
Metabolite changes	IIncreased 3-hydroxyisovaleric acid, increased 3-methylcrotonylglycine.
Gene	MCCA/MCCB
Gene location	3q25-q27, 5q12-q13.1
DNA testing available	Sequencing available internationally
DNA testing detail	No common mutations
Prenatal testing	May be possible for at-risk pregnancies using enzymatic analysis.
MS/MS Profile	C5:1 (tigyl or 3-methylcrotonyl carnitine) elevated C5-OH (3-hydroxy-2-methylbutyryl carnitine)- elevated
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=210200
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org